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10/510,652	10/28/2004	Steven K. Libutti	230809	4377

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EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	PAPER NUMBER
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,652	LIBUTTI ET AL.	
	Examiner	Art Unit	
	ANOOP SINGH	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed October 7, 2008 have been received and entered. Claims 1-25 have been cancelled. Claims 26-50 are pending.

Election/Restrictions

Applicant's election with traverse of the invention of claims 41-50 (group II) filed October 4, 2006 was acknowledged. The traversal was on the grounds that Examiner has not set forth convincing argument that the search and examination of all the groups necessarily represents an undue burden for the examiner. Applicant's argument for examining remaining claims drawn to a method of measuring the angiogenic activity of a test molecule by comparing the fluorescence vascular density were persuasive since both sets of group embrace methods of measuring angiogenic or anti angiogenic activity. Therefore, invention of claims 26-40 (group I) directed to a method of measuring angiogenic activity by comparing fluorescence vascular density assay were rejoined with elected inventions of group II for the examination purposes. Applicants have also elected polypeptide, synthetic molecule, fluorescein, XTT, serum and filter paper as species for claims readable on claims 26-50.

Claims 26-50 are currently under consideration.

Priority

It was noted that instant application is a 371 of PCT/US03/10932 filed on 04/09/2003 which claims benefit of 60/371,010 filed on 04/09/2002. However, upon review the disclosure of the prior-filed application, US provisional application 60/371,010, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. It is noted that 60/371,010 dated 4/9/2002 describes measuring angiogenic activity using fluorescence vascular density but does not show support for a method to determine angiogenic activity using XTT. Consequently, there is no written

description in application for using XTT or any other metabolic agent to determine angiogenic activity using spectrophotometer. In case, if applicants have evidence to support otherwise, applicants are invited to indicate page and line number for the written support as recited in claims 41-50 of the instant application. Therefore, the effective filing date for instant claims 41-50 is 04/09/2003 as subject matter of instant claims was described in the 60/371,010.

Maintained- Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 41-50 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Brooks et al: (Methods in Molecular Biology, 129, 257-269, IDS), Kurz et al (Developmental Dynamics, 1995, 203, 174-186), Frasca et al (Oncogene, 2001: 20, 3845-3856) and Kinnman et al (Lab Invest. 2001; 81(12): 1709-16, IDS) for the reasons of record.

Applicants' arguments and declaration filed October 7, 2008 have been fully considered but they are not fully persuasive. Applicants' argue that there are significant differences between Brdu based assay and the metabolic assay as claimed. Applicants assert that Brdu can be used with a cell specific antibody to discriminate cell type, while XTT is indiscriminate. Applicants also argue the difference between the method of detection between Brdu and XTT/MTT assay (see page 3 of the arguments). Applicants also assert that Frasca et al. used XTT to measure the proliferation of human thyroid cancer cells in matrigel, and Kinnman

et al. investigated the proliferation of hepatic stellate cells that were for homogenous cell cultures and not heterogeneous tissue.

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). As stated in previous office action, applicants agree that BrdU, XTT and MTT were commonly used assay to measure the proliferation of cells but differ with respect to their detection method. However, it is well established in case law that a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. In re Burkel, 201 USPQ 67 (CCPA 1979). Furthermore, in the determination of obviousness, the state of the art as well as the level of skill of those in the art are important factors to be considered.

In the instant case, prior to instant invention, use of proliferation-based assays was routine in the art to quantitate proliferation of endothelial cells. Applicants agree that Kurz provides an alternative method of measuring proliferation that is carried out utilizing cultured CAMs. Although, Kurz exemplified a method that differed from the claimed invention by not teaching administering an agent XTT or any other metabolic agent for measuring the metabolic activity in the test area. However, uses of XTT, MTT, WST-1or BrdU for measuring the cell proliferation was known to one of ordinary skill in the art at the time the claimed invention was made and these assays were routinely used in alternative to each other as evidenced by the teaching of Frasca and Kinnman. Although Brooks or Kurz et al did not use XTT, Kurz generally embraced potential of measuring proliferation assay to better measure and compare angiogenesis. In addition, Kurz provided adequate guidance for measuring proliferation of cells to measure the vessel density and length for quantitation of angiogenesis in CAM assay (supra). Applicants' argument that one of ordinary skill in the art would have

not used XTT to measure proliferation as Kinnman et al and Frasca both reported measuring proliferation in homogenous cell cultures is not persuasive. In fact, contrary to applicants' argument Frasca et al reported cell morphogenesis during angiogenesis could be determined by both a change in cell shape and an increase in cell number by using XTT assay (see page 3848, col .1, para. 1). Kinnman et al teaches that method of measuring mitochondrial reduction of the tetrazolium salt XTT to formazan to determine the number of viable, metabolically active cells (see page 1715, col. 1, para. 1). While Frasca and Kinnman both reported XTT assay in homogenous cell culture, however, they also reported that these assays are based on the ability of any metabolic active cells to reduce the tetrazolium salt XTT to orange colored compounds of formazan that could be measured with a spectrophotomete. The greater the number of active cells in the assay, the greater the activity of mitochondria enzymes, and the higher the concentration of the dye formed, which could then be measured and quantitated (see Kinnman et al, page 1715, col. 1, para. 1 and figure 5). Therefore, given that methods to measure proliferation of cell including XTT, MTT and Brdu were commercially available for determining the proliferation of EC during morphogenesis. It would have *prima facie* obvious to combine the prior art element of measuring proliferation by known methods of measuring the metabolic active cells to reduce the tetrazolium salt XTT to formazan in Kinnaman/Frasca. In the instant case, the combination would have yielded predictable results to one of ordinary skill in the art to determine cell proliferation/viability to measure cells density as an index of angiogenic activity in the method of Brooks with reasonable expectation of success to compare the metabolic activity of test agent to untreated control as a measure of relative angiogenic activity.

Applicants argue that that there are significant differences between BrdU and XTT in measuring proliferation of cells. Applicant's point that BrdU based

assay can be used with a cell specific antibody to discriminate the cell type, while XTT is indiscriminate.

In response, it is noted that Kurz et al show that BrdU can be incorporated into the newly synthesized DNA of replicating cells during the S-phase of the cell cycle by substituting for thymidine during DNA replication and using antibodies specific for BrdU can then be used to detect the incorporated chemical indicating cells that were actively replicating their DNA (see page 177, col.1, para. 3 and page 175, col. 2, last para.). Based on preceding discussion it is apparent that Kurz emphasized the importance of measuring the proliferating cells in CAM to measure the angiogenic index. In response to the applicants' assertion and evidence (see Folkman et al exhibit A) that cell other then endothelial cells are also involved during angiogenesis, it is emphasized that Brdu staining reported by Kurz et al is not limited to endothelial cell rather it is be incorporated into the newly synthesized DNA of replicating cells of different origin during the S-phase of the cell cycle. Thus, Brdu assay of proliferation in CAM assay would not be limited to any specific endothelial cell population, rather it is based on measuring in the number of cells in a population that are actively synthesizing DNA which is a measure of number of actively proliferating cell in a population. The Examiner has only indicated that BrdU method taught by Kurz could also be used to further characterize the cell type and exact role of cell type in angiogenesis using histology or double staining at, but this does not negate the fact that instant method of Kurz emphasized measuring proliferation in CAM to measure the extent of angiogenesis. Therefore, given that many methods to measure proliferation of cell such as XTT, MTT or Brdu were commercially available, it would have been obvious for one of ordinary skill in the art to for to use other known method of measuring proliferation of cells such as method that use metabolic agent to determine cell viability/proliferation in order to determine the density of proliferating cells as an index of angiogenic activity in the method of Brooks with reasonable expectation of success. Thus, cited art provide

evidence that extensive proliferation of cells in capillary tube in CAM around ~8-10 post incubation, therefore, any method that measure number of cells in capillary network of CAM would extrapolate to extent of angiogenesis.

Applicants' argument of demonstrated surprising results in showing that metabolic substrates, such as XTT, do not discriminate between cell types (see page 4, last para. of the arguments) is not persuasive because all the metabolic assays including XTT is based on the ability of any metabolic active cells to reduce the tetrazolium salt XTT to formazan. The intensity of formazan product could be measured with a spectrophotometer to determine the number of active cells in the area. The results would not be surprising as one of ordinary skill in the art would expect any type of cell that is metabolically active to reduce the tetrazolium salt XTT to formazan. Applicants have not provided any evidence that compare that method that uses XTT or MTT will be any different that other methods of measuring cellular viability and/or proliferation.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 26-40 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Brooks et al; (Methods in Molecular Biology, 129, 257-269, IDS), Iruela-Arispe et al (Circulation. 1999; 100:1423-1431), and Rizzo et al (Microvascular Res, 1995, 49, 49-63, IDS).

Applicants' arguments filed October 7, 2008 have been fully considered but are not persuasive. Applicants assert that one of ordinary skill in the art at the time of the invention would have no reason to believe that quantitative analysis of a three-dimensional digital image of the vasculature within the CAM would provide superior results over a two-dimensional method. Applicants argue that Iruela-Arispe et al injected FITC-dextran into the circulation of the CAM to evaluate

vertical vessel growth into a collagen gel placed on top of the CAM by collecting a two-dimensional image of the collagen gel and measuring overall fluorescence. The skilled artisan would have had no motivation to collect a three dimensional image (see page 5 of the argument).

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). With respect to applicants' argument of two or three dimensional imaging, it is noted that one of ordinary skill in the art would modify the method of Brooks to measure angiogenic or anti angiogenic activity in a CAM assay by measuring fluorescent vascular density by directly injecting the FITC-dextran into the circulation of the CAM as disclosed by Iruela-Arispe with a reasonable expectation of success particularly since it is disclosed that the degree of fluorescence intensity parallels variations in capillary density. It is noted that Iruela-Arispe is applied to the extent, it was known to one of ordinary skill in the art that FITC-dextran could be microinjected to determine the vascular density in CAM to compare the angiogenic or anti angiogenic activity. In the instant case, all the claimed elements were known in prior art and one skilled in the art could have modified the method by combining the method of Brooks by injecting FITC-dextran into CAM area elements as disclosed by Iruela-Arispe to determine FVD by known methods of Rizzo that would have provided 3 dimensional pictures comprising plurality of pixel to digitally quantify the pixel to obtain FVD with no change in their respective function . Iruela-Arispe /Rizzo et al had already described use of FITC-dextran to measure the bio distribution in neo vasculature in CAM that could have been used as for quantitation to compare angiogenic or anti angiogenic activity. Thus, it would have only required the routine experimentation to modify the method disclosed by Brooks, Iruela-Arispe and Rizzo to include capture the

image with CLCM comprising plurality of pixel to digitally quantify the plurality of pixel from the 3 dimensional image to obtain FVD to measure angiogenic or anti angiogenic activity as required by instant invention. It is noted that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, -- USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396).

In response to the applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, applicants' arguments and secondary evidence are not commensurate with the scope of the claims. It is noted that base claims are not restricted to use of FITC-dextran as argued by the applicants. Additionally, although Rizzo et al studied that extravasation of FITC-Dextran using 3-dimensional imaging, but it is emphasized that Rizzo et al also disclose imaging the interstitial accumulation of FITC- Dextran (Fig. 4). Contrary to applicants' assertion it is not instant specification, rather it is the prior art that provided adequate guidance with respect to measuring accumulated FITC-dextran. It is noted that Rizzo et al disclose that the tissue plane containing the CAM capillary networks is separated from that containing the first-order micro vessels by a distance of less then 5 μm, optical dissection of the tissue planes is well within the theoretical z resolution (1 <mm) of the confocal system. Following each microinjection, randomly selected fluorescent confocal images of the respective tissue planes is captured by the image-analysis software at 2, 5, 7, 10, and 15 rain

for play-back analysis (see page 51, para. 2 and 3). Additionally, Rozzo et al teach quantitation of changes in intensity by recording fluorescent images that are digitized for quantitative assessment of fluorescent intensity. The digitized images are composed of pixels of varying brightness depending on respective pixel light intensity (gray-scale levels ranged from 0 to 255) meeting the limitation of claims 37-40. Furthermore, mean values different capillaries are calculated for the comparison of the data (see page 51, para. 4 and 5). The results of Rizzo et al provide evidence that method to capture 3 dimensional image from the test region comprising plurality of pixels and digitally quantifying the plurality of the pixel to obtain the fluorescence density was known in prior art to investigate the vasculature (see page 62, last two lines). Given that Iruela-Arispe /Rizzo et al had already described use of FITC-dextran to measure the bio distribution in neo vasculature in CAM that could have been used as for quantitation to compare angiogenic or anti angiogenic activity. Thus, it would have only required routine experimentation to modify the method disclosed by Iruela-Arispe /Brooks and Rizzo to include capture the image with CLCM comprising plurality of pixel to digitally quantify the plurality of pixel from the 3 dimensional image to obtain FVD to measure angiogenic or anti angiogenic activity as required by instant invention.

Applicants cite the declaration of Dr. Cuttitta to assert the commercial success based on recognition of superior results and use of instant method in wet lab course offered by FAES, NIH, Bethesda as evidence of commercial success (See page 4, section 9 and 10 of the declaration filed 3/19/2008 and arguments on page 6, last para.). Applicants argue that this commercial success is directly related to superior results of the assay over the other methods previously used.

Applicants' arguments and declaration is again acknowledged but are not fully persuasive. In the instant case, applicants have asserted that "use of instant method in wet lab course offered by FAES, NIH, is summarized". However, recitation of success of the claimed method being taught at one institution is not a

hard evidence of commercial success of a claimed method using an instant method for high throughput screening. Applicants' assertions of improved and superior result are not commensurate with the scope of the claim. In the instant case, it is unclear which method that uses specific concentration of specific fluorescent molecule covered by the commercial success particularly since pending claims are broad and embraces several variables as disclosed in this application and declaration (including injection site, needle size, type and size of fluorescent molecule). The assertion does not provide any hard evidence or nexus between collaborative partners, licensees to the claimed method using any specific method that uses specific method steps commensurate with full scope of the claims. MPEP 716.03 states "[A]n applicant who is asserting commercial success to support its contention of nonobviousness bears the burden of proof of establishing a nexus between the claimed invention and evidence of commercial success". In addition "Objective evidence of nonobviousness including commercial success must be commensurate in scope with the claims. *In re Tiffin, 448 F.2d 791, 171 USPQ 294 (CCPA 1971)*". It is noted that although applicants assert use of wet lab course at FAES using this technology, however, recitation of success of the claimed technology in terms use of instant method in wet lab course offered by FAES is not a hard evidence of commercial success. It is emphasized that offering course at wet lab does not show market share of the product, nor does it provide any comparative sales totals that would be normally expected from a similar kind of product. MPEP 716.03(b) [R-2] IV states "Gross sales figures do not show commercial success absent evidence as to market share, *Cable Electric Products, Inc. v. Genmark, Inc.*, 770 F.2d 1015, 226 USPQ 881 (Fed. Cir. 1985), or as to the time period during which the product was sold, or as to what sales would normally be expected in the market, *Ex parte Standish*, 10 USPQ2d 1454 (Bd. Pat. App. & Inter. 1988).

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 41-50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Brooks et al; (Methods in Molecular Biology, 129, 257-269, IDS), Kurz et al (Developmental Dynamics, 1995, 203, 174-186), Yasukawa et al (Invest Ophthalmology Vis Sci, 1999, 40: 2690-2696) and Woltering et al (US Patent 6,893,812, dated 5/17/2005, filed 5/25/2001, effective filing 5/30/2000).

Applicants' arguments filed October 7, 2008 have been fully considered but are not persuasive. Applicants argue that they have demonstrated surprising results in showing that metabolic substrates, such as XTT, which do not discriminate between cell types, could be used in the CAM assay to monitor the affect of angiogenic and anti-angiogenic agents on proliferation. Applicants also assert that Woltering et al disclosed the use of MTT assays in their angiogenesis assay involving placement of a tumor discs into a matrix, they do not teach 1) that it has any utility in measuring proliferation or that it could be used in a heterogeneous tissue. Applicants assert that they recite MTT assays for measuring "cellular viability" rather than proliferation. Applicants argue Woltering et al clearly recognized that the assay would be non-discriminatory and would not give data specific for angiogenesis, since the tumors would likely be proliferating also.

In response, it appears that Applicant is arguing that the cited references do not expressly suggest the claimed invention. However, it is well established in case law that a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. In re Burkel, 201 USPQ 67 (CCPA 1979). Furthermore, in the determination of obviousness, the states of the art as well as the level of skill of those in the art are important factors to be considered. The teaching of the cited references must be viewed in light of these factors. It also appears that applicant is attempting to attack each reference individually. However, in a 103 rejection the references must be considered as a whole. In the instant case, Applicants' argument that cited reference teaches MTT assays for

measuring "cellular viability" rather than proliferation is not persuasive. As stated in the preceding section, XTT assay is based on the ability of metabolic active cells to reduce the tetrazolium salt XTT to formazan . The intensity could be read with a spectrophotometer and the intensity of the dye is proportional to the number of metabolic active cells. The greater the number of active cells in the well, the greater the activity of mitochondria enzymes, and the higher the concentration of the dye formed, which can then be measured and quantitated. Applicants have argued about the importance of non-discriminatory measurements of a cell to determine the angiogenic index (see applicants' argument page 4, para. 2). Contrary to applicants' argument Woltering et al provided guidance with respect to methods to evaluate neo-vessel proliferation/promotion by measuring cellular viability using any of various methods known in the art including colorimetric assay to measure the metabolic activity of cells in a tissue fragment. Woltering et al embraced the potential of measuring angiogenesis by determining the total surface area as a function of time, the rate of change may be determined (see col. 10, lines 30-39).

Therefore, given that methods to measure XTT, or Brdu were available, it would have been obvious for one of ordinary skill in the art to use a known method of measuring metabolically active cells that are responsible for angiogenesis (fibroblast, SMC, endothelial) such as method that use metabolic agent to determine cell viability/proliferation in order to determine the density of cells as an index of angiogenic activity in the method of Brooks with a reasonable expectation of success. It is noted that the one of ordinary skill in the art would have further motivated to optimize the treatment routes, regimen and would have to optimize the steps of administering test molecule and agent to measure metabolic activity in different vessel depending upon total volume of test agent required for the angiogenic or anti angiogenic response as per the teachings of Brooks (see MPEP 2144.04). One who would practiced the invention would have had reasonable expectation of success because Brooks had already a method to measure angiogenic

or anti angiogenic agent activity in a CAM assay using the XTT/MTT or Brdu assay to determine the number of cell patterns during morphogenesis that could have been used as for quantitation to compare angiogenic or anti angiogenic activity. Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26-50 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-34 of copending Application No. 11/014472.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of measuring the angiogenic or anti angiogenic activity of a test molecule in a CAM

assay by administering a fluorescent-labeled particle and measuring the FVD value or by using an agent that has metabolic activity and measure spectrophotometer reading to determine angiogenic activity. Since the specification and claims of the '472, application contemplated same test molecule and fluorescent-labeled particle or by using XTT and embraced same method steps in CAM assay as one disclosed in instant application. Thus, the claims of application no 11/014472 differs only with respect to a narrower scope of test molecule that is obtained from an animal that could be used in the method as claimed in an instant application.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

It is noted that applicants have indicated that instant rejection would be addressed once claims are found allowable in either application.

Conclusion

No Claims allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Coagswell et al SPIE Vol. 2184 Three-Dimensional Microscopy , 1994, 49-54) teaches method of using 3 dimensional LSM to digitally quantify the fluorescence form a image.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANOOP SINGH whose telephone number is (571)272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anoop Singh
AU 1632
/Valarie Bertoglio/
Primary Examiner, Art Unit 1632